New Cerebral Protection System for TAVR: The ProtEmbo® System

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Disclosure

Speaker's name : Professor Nikos Werner

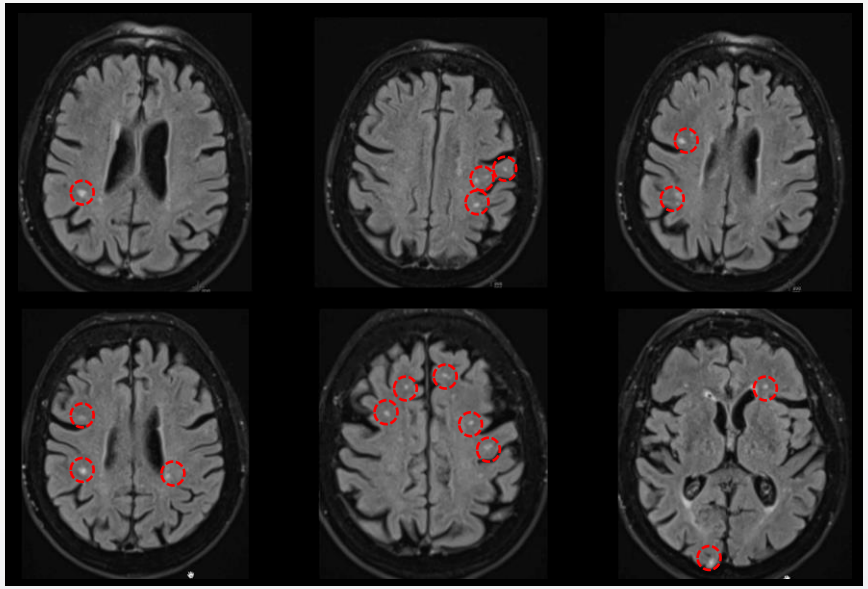
☑ I have the following potential conflicts of interest to declare:

Receipt of grants / research support: Abiomed, Shockwave

Receipt of honoraria or consultation fees: Abiomed, Boston Scientific, Edwards Lifesciences, Medtronic, Protembis, Shockwave

Background

- Stroke remains the most feared and harmful complications of TAVR
- New cerebral lesions occur in 70% - 90% of TAVR recipients

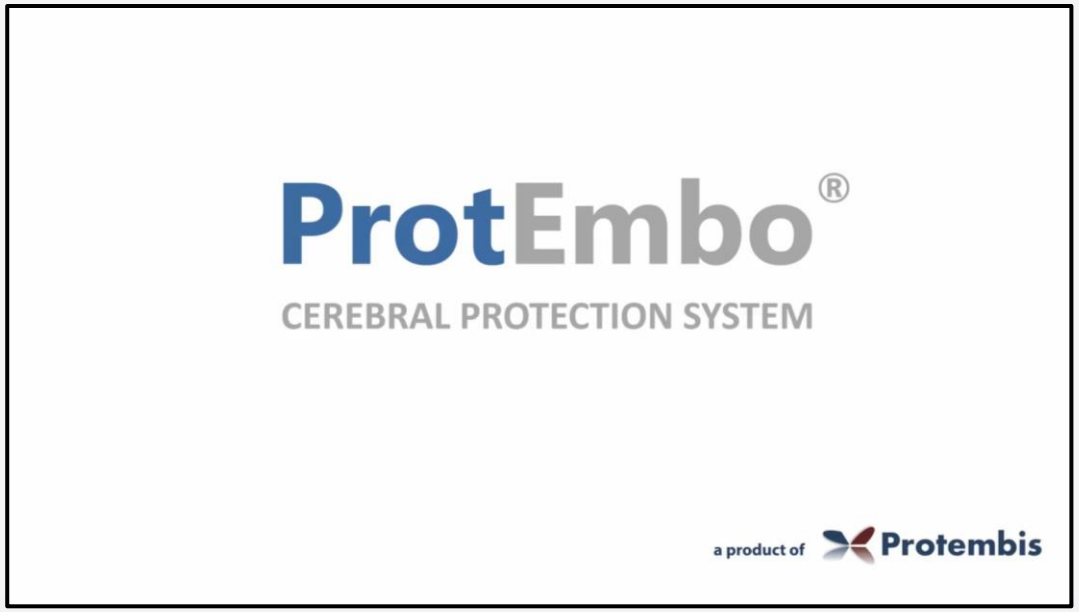


- Delirium
- Cognitive decline
- Up to 4-fold risk of future stroke
- >3-fold risk of mortality
- >2-fold risk of dementia

Sources:
Kahlert et al Circulation.2010;121:870-878.
Barber PA, et al. Cerebral ischemic lesions on diffusion-weighted imaging are associated with neurocognitive decline after cardiac surgery. Stroke 2008;39:1427–1433.
Sigurdsson S, et al. Incidence of brain infarcts, cognitive change, and risk of dementia in the general population. Stroke 2017;48:2353–2360
Pagnesi 2016, Sacco 2013, Vermeer 2009 and 2003.

The ProtEmbo Cerebral Protection System

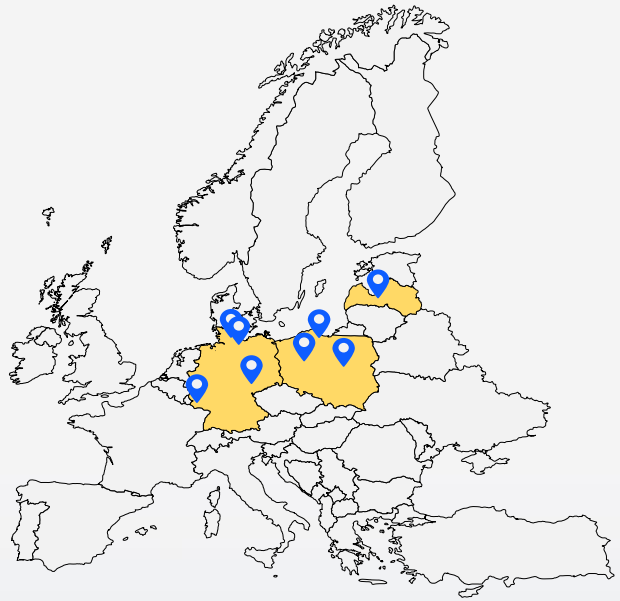
- Protects all 3 vessels to the brain
- Smallest filter pores – 60 µm
- Intuitive design and simple handling
- Quick implantation time – mean 4.7 mins (SD ± 4.4 mins)
- Smallest 6 Fr profile device deployed via left radial artery to reduce access site complications
- Low profile footprint in aortic arch to minimize interference with the TAVR procedure
- Heparin coating for optimal blood compatibility



The PROTEMBO C Trial

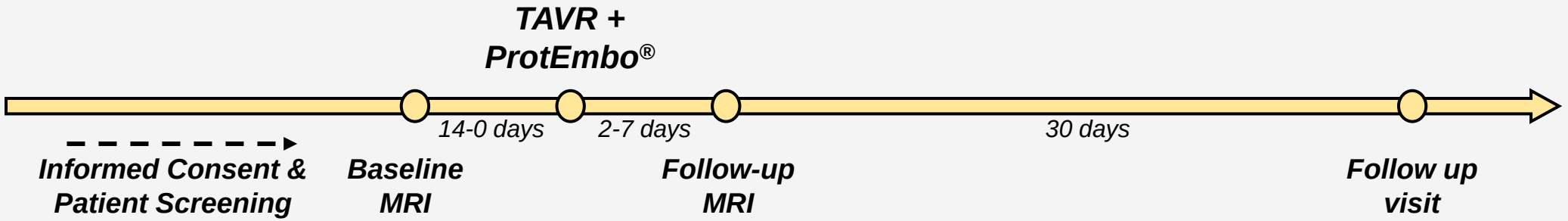
- Multi-center, single-arm, exploratory study of safety and performance of the ProtEmbo® Version 2.0.
- Independent DSMB & Core labs for imaging, angiography & histopathology
- 64 patients enrolled at 8 clinical sites in Germany, Poland and Latvia

Primary Endpoints	***Safety***	**MACCE at 30 days**
	Performance	**Technical success including device related safety outcomes**
Secondary Endpoint	***Efficacy***	**Reduction of new DW-MRI lesions; rate of death or all stroke**

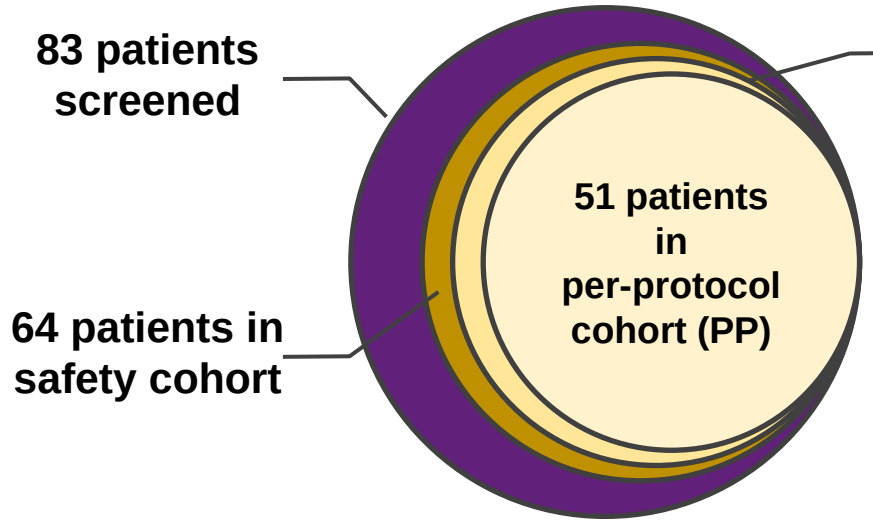


The PROTEMBO C Trial

Schedule of Events:



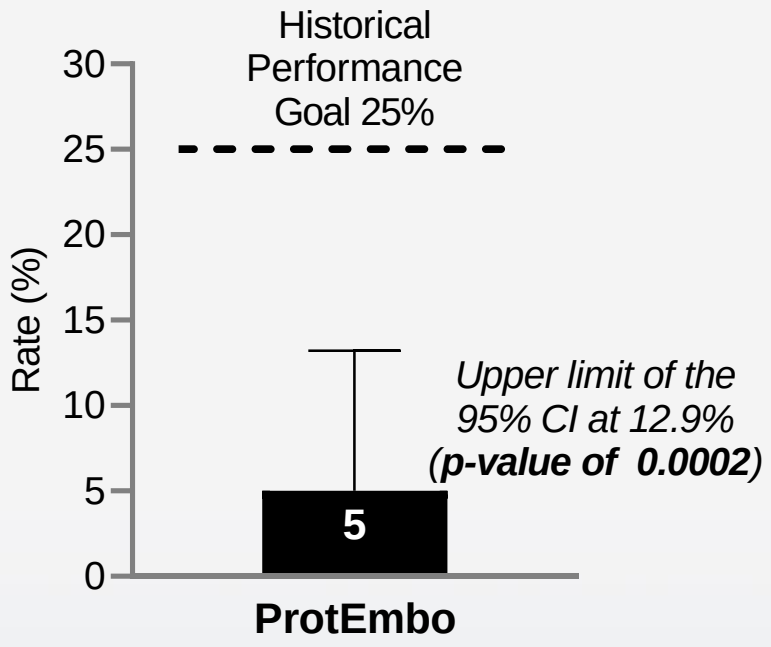
Study Cohorts:



Safety: *Pts with baseline MRI*
ITT: *Pts who met incl. criteria & with intention-to-treat*
PP: *Pts treated per protocol incl. follow up MRI*

Primary Safety Endpoint

Primary Safety endpoint[1]; MACCE at 30-days < pre-specified historical performance goal

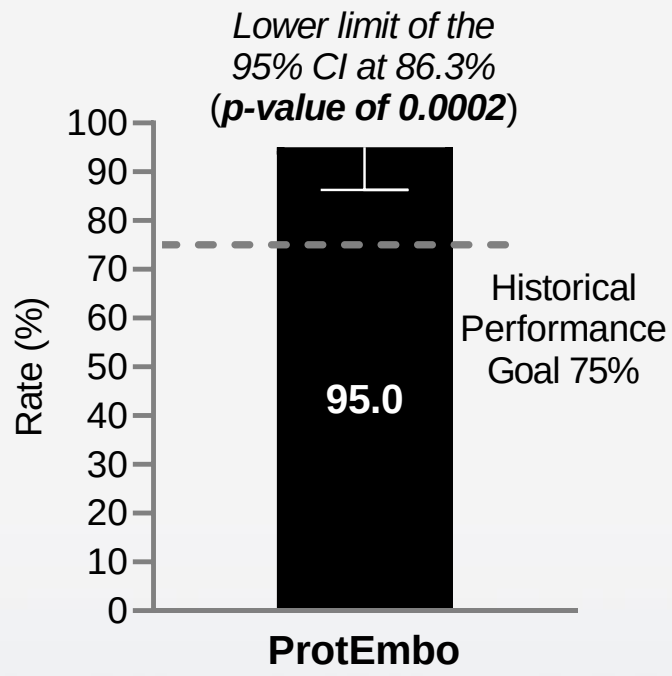


30 Day Safety Outcomes	N=60
Any MACCE, % (k/n)	**5 (3/60)**
All-cause mortality	0 (0/60)
All stroke	1.7 (1/60)[2]
AKI (stage 2 or 3)	1.7 (1/60)[3]
Life threatening or disabling bleeding	1.7 (1/60)[4]
Major vascular complications,	0 (0/60)
Procedure related vascular complications	6.7 (4/60)[5]

1. ITT cohort included 60 patients; the ITT cohort of 60 patients was decisive for primary safety endpoint analysis (rate of 5% also significantly below PG). 2. Minor cerebral infarct 12h post TAVR in a patient of the ITT cohort (N=60) in whom ProtEmbo was removed prematurely, and no cerebral protection was used during part of TAVR procedure (2-times post-dilatation of the valve prosthesis). 3. Patient suffered from chronic renal insufficiency prior to procedure. 4. Cardiac tamponade as a result of TAVR and pericardial drainage. 5. No MACCE events, 4 symptomatic events in 60 patients in ITT cohort.

Primary Performance Endpoint

Primary performance endpoint[1]. Success above pre-specified historical performance goal



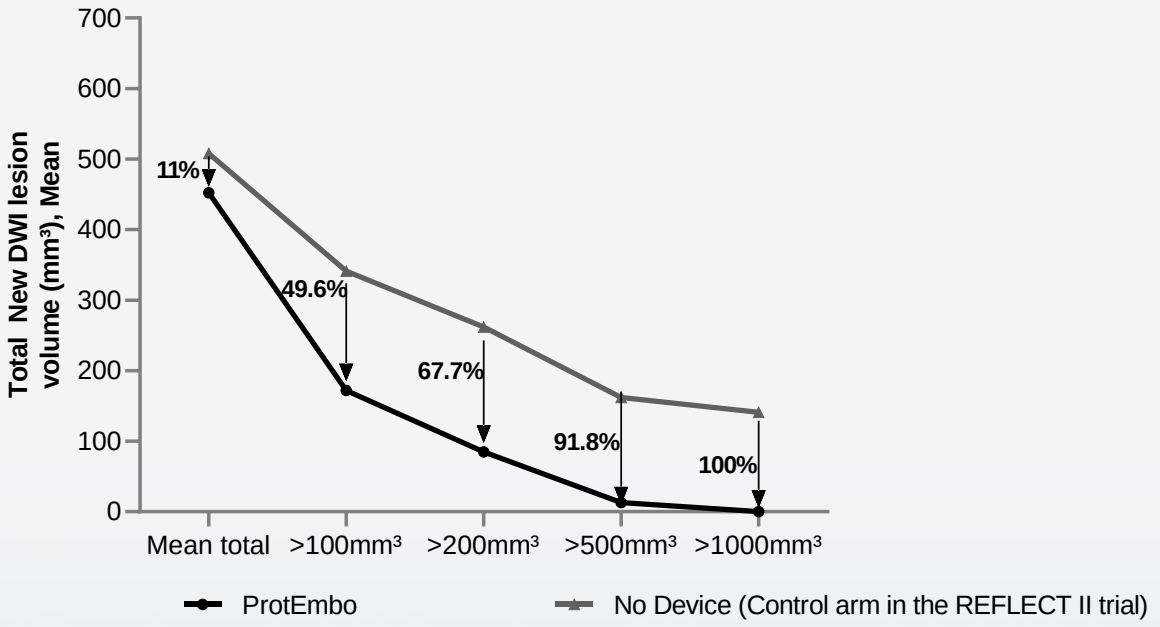
Performance Characteristics	N=60
Technical Success, % (k/n)	**95 (57/60)**
Delivery and deployment in aortic arch, % (k/n)	96.7 (58/60)
Stability and coverage of cerebral vessels, % (k/n)	98.3 (57/58)[2]
Removal, % (k/n)	100 (60/60)
Time to place device (min), Mean ± SD	4.7 ± 4.4[3]
Additional contrast use (ml), Mean ± SD As % of TAVR	4.3 ± 13.7[4] 2.7%
Additional fluoro time (min), Mean ± SD As % of TAVR	4.8 ± 4.1[5] 20%

1. N=60 patients in ITT cohort for primary performance endpoint analysis

Secondary Efficacy Analysis: DW MRI

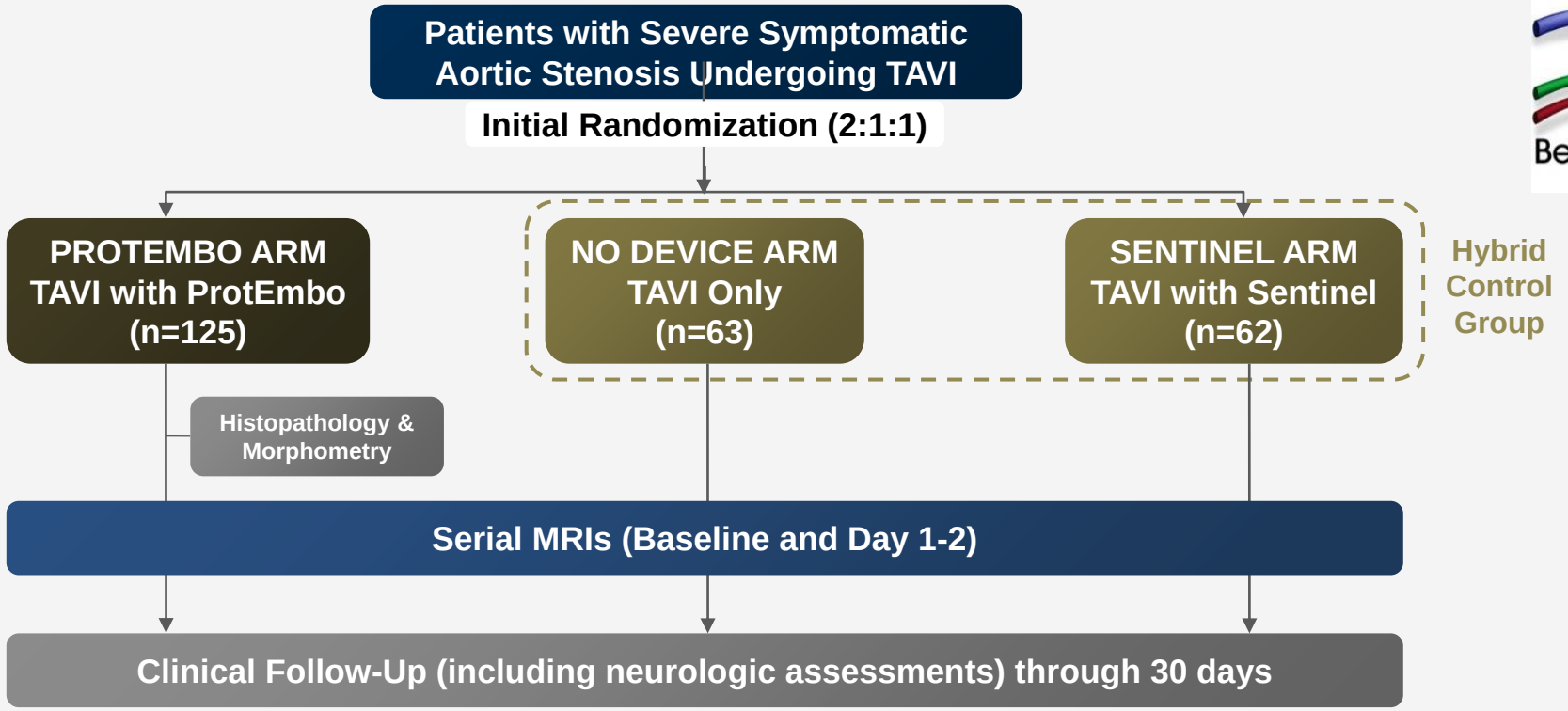
	Per Protocol Cohort (N=51)
Days following TAVR (days), Mean ± SD	4.9 ± 1.4
Total New DWI lesion volume, (mm^3), Median (IQR)	**210 (108, 566)**
Total New DWI lesion volume, (mm^3), Mean ± SD	452 ± 606
Average New DWI lesion volume, (mm^3), Median (IQR)	39 (25, 61)
Single New DWI lesion volume, (mm^3), Median (IQR)	30 (18, 57)
Number of New lesions, #, Median (IQR)	7 (3, 13)
Freedom of brain lesions > 150 mm^3, % (k/n)	**76.5% (39/51)**
Freedom of brain lesions > 350 mm^3, % (k/n)	**94.1% (48/51)**

Significant reduction in total new lesion volume (TNLV) vs historical control group[1].



1. Nazif TM, Moses J, Sharma R, Dhoble A, Rovin J, Brown D, Horwitz P, Makkar R, Stoler R, Forrest J, Messé S, Dickerman S, Brennan J, Zivadinov R, Dwyer MG, Lansky AJ; REFLECT II Trial Investigators. Randomized Evaluation of TriGuard 3 Cerebral Embolic Protection After Transcatheter Aortic Valve Replacement: REFLECT II. JACC Cardiovasc Interv. 2021 Mar 8;14(5):515-527. doi: 10.1016/j.jcin.2020.11.011. Epub 2021 Mar 1. PMID: 33663779.

Approved ProtEmbo IDE Trial – Adaptive Study Design



Adaptive study design with group sequential boundaries to assess outcomes at sequential interim analyses; First interim analysis at 250 patients with decision about conduct of trial based on predefined definitions of success or futility (by independent DSMB). After 250 patients further interim analyses will be conducted each time on 50 additional patients to complete with study up to maximum of 500 patients. 510(k) clearance based on superiority versus No Device Arm/ Hybrid Control Group.

Conclusion

- Primary safety and performance endpoints of the PROTEMBO C Trial achieved with statistical significance.
- Secondary efficacy analysis reveals low rate of new lesions and no large single lesions
- Pivotal IDE trial approved by FDA has been initiated: Primary endpoint is DW-MRI assessment at 24±12 hours to evaluate safety & efficacy of next generation ProtEmbo® System (V3.0)